

FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4270001	APPLICATION NO. 09/065,902 <b>JUL 29 1998</b>
	APPLICANT TANZI and KIM <b>GROUP 1800</b>	
	FILING DATE April 24, 1998	GROUP <b>1643/1644</b>

U.S. PATENT DOCUMENTS							
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
<i>KC</i>	AR	1	Borchelt, D.R., et al., "Familial Alzheimer's Disease-Linked Presenilin 1 Variants Elevate Aβ1-42/1-40 Ratio In Vitro and In Vivo," <i>Neuron</i> 17:1005-1013 (November 1996)
<i>KC</i>	AS	1	Bush, A.I., et al., "An Abnormality of Plasma Amyloid Protein Precursor in Alzheimer's Disease," <i>Annals of Neurology</i> 32:57-65 (1992)
<i>KC</i>	AT	1	Chinnaiyan, A.M., and Dixit, V.M., "The cell-death machine," <i>Current Biology</i> 6:555-562 (May 1996)

EXAMINER <i>Karen Clemens</i>	DATE CONSIDERED <i>3/20/00</i>
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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KC	AR	2	Ciechanover, A., "The Ubiquitin-Proteasome Proteolytic Pathway," <i>Cell</i> 79:13-21 (1994)
KC	AS	2	Citron, M., et al., "Mutant presenilins of Alzheimer's disease increase production of 42-residue amyloid $\beta$ -protein in both transfected cells and transgenic mice," <i>Nature Medicine</i> 3:67-72 (January 1997)
KC	AT	2	Cook, D.G., et al., "Expression and analysis of presenilin 1 in a human neuronal system: Localization in cell bodies and dendrites," <i>Proc. Natl Acad. Sci. USA</i> 93:9223-9228 (August 1996)

EXAMINER <i>Karen Clemens</i>	DATE CONSIDERED 3-20-00
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JUL 29 1998

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

KC	AR	3	Cotman, C.W., and Anderson, A.J., "A Potential Role for Apoptosis in Neurodegeneration and Alzheimer's Disease," <i>Molecular Neurobiology</i> 10:19-45 (1995)
KC	AS	3	Deng, G., et al., "Alzheimer-associated presenilin-2 confers increased sensitivity to apoptosis in PC12 cells," <i>FEBS Letters</i> 397:50-54 (November 1996)
KC	AT	3	Doan, A., et al., "Protein Topology of Presenilin 1," <i>Neuron</i> 17:1023-1030 (November 1996)

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KC	AR	4	Duff, K., et al., "Increased amyloid- $\beta$ 42(43) in brains of mice expressing mutant presenilin 1," <i>Nature</i> 383:710-713 (October 1996)
KC	AS	4	Fenteany, G., et al., "Inhibition of Proteasome Activities and Subunit-Specific Amino-Terminal Threonine Modification by Lactacystin," <i>Science</i> 268:726-731 (1995)
KC	AT	4	Finley, D., and Chau, V., "Ubiquitination," <i>Annu. Rev. Cell Biol.</i> 7:25-69 (1991)

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KC	AR	5	Forloni, G., et al., "Apoptosis mediated neurotoxicity induced by chronic application of $\beta$ amyloid fragment 25-35," <i>NeuroReport</i> 4:523-526 (1993)
KC	AS	5	Guo, Q., et al., "Alzheimer's PS-1 mutation perturbs calcium homeostasis and sensitizes PC12 cells to death induced by amyloid $\beta$ -peptide," <i>NeuroReport</i> 8:379-383 (December 1996)
KC	AT	5	Goldberg, Y.P., et al., "Cleavage of huntingtin by apopain, a proapoptotic cysteine protease, is modulated by the polyglutamine tract," <i>Nature Genetics</i> 13:442-449 (August 1996)

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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>KC</i>	AR	<u>6</u>	Gossen, M., and Bujard, H., "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters," <i>Proc. Natl. Acad. Sci. USA</i> 89:5547-5551 (1992)
<i>KC</i>	AS	<u>6</u>	Hochstrasser, M., "Ubiquitin, proteasomes, and the regulation of intracellular protein degradation," <i>Curr. Opin. Cell Biol.</i> 7:215-223 (1995)
<i>KC</i>	AT	<u>6</u>	Hochstrasser, M., "Protein Degradation or Regulation: Ub the Judge," <i>Cell</i> 84:813-815 (March 1996)

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<i>KC</i>	AR	Z	Inoue, S., et al., "Inhibition of Degradation of 3-Hydroxy-3-methylglutaryl-coenzyme A Reductase in Vivo by Cysteine Protease Inhibitors," <i>J. Biol. Chem.</i> 266:13311-13317 (1991)
<i>KC</i>	AS	Z	Jacobson, M.D., et al., "Programmed Cell Death in Animal Development," <i>Cell</i> 88:347-354 (February 1997)
<i>KC</i>	AT	Z	Jensen, T.J., et al., "Multiple Proteolytic Systems, Including the Proteasome, Contribute to CFTR Processing," <i>Cell</i> 88:129-135 (1995)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

KC	AR	8	Johnson, E.M., Jr., "Possible Role of Neuronal Apoptosis in Alzheimer's Disease," <i>Neurobiology of Aging</i> 15 (Suppl. 2):S187-S189 (1994)
KC	AS	8	Kim, T.-W., et al., "Proteolytic Processing and Ubiquitin-Dependent Degradation of Alzheimer-Associated Presenilin 1 and 2," <i>Soc. Neurosci. Abstr.</i> 22:727, Abstract No. 293.5 (November 1996)
KC	AT	8	Kim, T.-W., et al., "Endoproteolytic Cleavage and Proteasomal Degradation of Presenilin 2 in Transfected Cells," <i>J. Biol. Chem.</i> 272:11006-11010 (April 1997)

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	FILING DATE April 24, 1998	GROUP 1643/664

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	AL						Yes No
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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

KC	AR	2	Kim, T.-W., et al., "Alternative Cleavage of Alzheimer-Associated Presenilins During Apoptosis by a Caspase-3 Family Protease," <i>Science</i> 277:373-376 (July 1997)
KC	AS	2	Koo, E.H., and Squazzo, S.L., "Evidence That Production and Release of Amyloid $\beta$ -Protein Involves the Endocytic Pathway," <i>J. Biol. Chem.</i> 269:17386-17389 (1994)
KC	AT	2	Kovacs, D.M., et al., "Alzheimer-associated presenilins 1 and 2: Neuronal expression in brain and localization to intracellular membranes in mammalian cells," <i>Nature Medicine</i> 2:224-229 (February 1996)

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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
KC	AR	10	L'Hernault, S.W., and Arduengo, P.M., "Mutation of a Putative Sperm Membrane Protein in <i>Caenorhabditis elegans</i> Prevents Sperm Differentiation but Not Its Associated Meiotic Divisions," <i>J. Cell Biol.</i> 119:55-68 (1992)
KC	AS	10	LaFerla, F.M., et al., "The Alzheimer's A $\beta$ peptide induces neurodegeneration and apoptotic cell death in transgenic mice," <i>Nature Genetics</i> 9:21-30 (1995)
KC	AT	10	LeBlanc, A., "Apoptosis and Alzheimer's Disease," in <i>Molecular Mechanisms of Dementia</i> , Wasco, W., and Tanzi, R.E., eds., Humana Press, Totowa, NJ, pp. 57-71 (November 1996)

EXAMINER <span style="font-family: cursive; font-size: 1.2em;">Karen Clemen</span>	DATE CONSIDERED <span style="font-family: cursive; font-size: 1.2em;">3/25/00</span>
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	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

KC	AR	11	Lee, M.K., et al., "Expression of Presenilin 1 and 2 (PS1 and PS2) in Human and Murine Tissues," <i>J. Neurosci.</i> 16:7513-7525 (December 1996)
KC	AS	11	Levitan, D., and Greenwald, I., "Facilitation of <i>lin-12</i> -mediated signalling by <i>sel-12</i> , a <i>Caenorhabditis elegans</i> <i>S182</i> Alzheimer's disease gene," <i>Nature</i> 377:351-354 (1995)
KC	AT	11	Levy-Lahad, E., et al., "Candidate Gene for the Chromosome 1 Familial Alzheimer's Disease Locus," <i>Science</i> 269:973-977 (1995)

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KC	AR	12	Li, X., and Greenwald, I., "Membrane Topology of the C. elegans SEL-12 Presenilin," <i>Neuron</i> 17:1015-1021 (November 1996)
KC	AS	12	Martin, S.J., and Green, D.R., "Protease Activation during Apoptosis: Death by a Thousand Cuts?," <i>Cell</i> 82:349-352 (1995)
KC	AT	12	McGee, T.P., et al., "Degradation of 3-Hydroxy-3-methylglutaryl-CoA Reductase in Endoplasmic Reticulum Membranes is Accelerated as a Result of Increased Susceptibility to Proteolysis," <i>J. Biol. Chem.</i> 271:25630-25638 (October 1996)

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KC	AR	13	Page, K., et al., "In situ hybridization analysis of presenilin 1 mRNA in Alzheimer disease and in lesioned rat brain," <i>Proc. Natl. Acad. Sci. USA</i> 93:14020-14024 (November 1996)
KC	AS	13	Pai, J.-T., et al., "Purification and cDNA cloning of a second apoptosis-related cysteine protease that cleaves and activates sterol regulatory element binding proteins," <i>Proc. Natl. Acad. Sci. USA</i> 93:5437-5442 (May 1996)
KC	AT	13	Paradis, E., et al., "Amyloid $\beta$ Peptide of Alzheimer's Disease Downregulates Bcl-2 and Upregulates Bax Expression in Human Neurons," <i>J. Neurosci.</i> 16:7533-7539 (December 1996)

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KC	AR	14	Perez-Tur, J., et al., "A mutation in Alzheimer's disease destroying a splice acceptor site in the presenilin-1 gene," <i>NeuroReport</i> 7:297-301 (1995)
KC	AS	14	Rock, K.L., et al., "Inhibitors of the Proteasome Block the Degradation of Most Cell Proteins and the Generation of Peptides Presented on MHC Class I Molecules," <i>Cell</i> 78:761-771 (1994)
KC	AT	14	Rogaev, E.I., et al., "Familial Alzheimer's disease in kindreds with missense mutations in a gene on chromosome 1 related to the Alzheimer's disease type 3 gene," <i>Nature</i> 376:775-778 (1995)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

<i>KC</i>	AR	<u>15</u>	Roitelman, J., et al., "Immunological Evidence for Eight Spans in the Membrane Domain of 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase: Implications for Enzyme Degradation in the Endoplasmic Reticulum," <i>J. Cell Biol.</i> 117:959-973 (1992)
<i>KC</i>	AS	<u>15</u>	Sakai, J., et al., "Sterol-Regulated Release of SREBP-2 from Cell Membranes Requires Two Sequential Cleavages, One Within a Transmembrane Segment," <i>Cell</i> 85:1037-1046 (June 1996)
<i>KC</i>	AT	<u>15</u>	Schellenberg, G.D., "Genetic dissection of Alzheimer disease, a heterogeneous disorder," <i>Proc. Natl. Acad. Sci. USA</i> 92:8552-8559 (1995)

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Page 16 of 21  
 JUL 29 1998

FORM PTO-1449  INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4270001	APPLICATION NO. 09/065,902
	APPLICANT TANZI and KIM	
	FILING DATE April 24, 1998	GROUP 1643 1.44

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
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<i>KC</i>	AR	<u>16</u>	Scheuner, D., et al., "Secreted amyloid $\beta$ -protein similar to that in the senile plaques of Alzheimer's disease is increased <i>in vivo</i> by the presenilin 1 and 2 and APP mutations linked to familial Alzheimer's disease," <i>Nature Medicine</i> 2:864-870 (August 1996)
<i>KC</i>	AS	<u>16</u>	Sherrington, R., et al., "Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease," <i>Nature</i> 375:754-760 (1995)
<i>KC</i>	AT	<u>16</u>	Sutcliffe, J.G., et al., "Antibodies That React with Predetermined Sites on Proteins," <i>Science</i> 219:660-666 (1983)

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	APPLICANT TANZI and KIM	
	FILING DATE April 24, 1998	GROUP 1643 / 1800

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KC	AS	17	Thinakaran, G., et al., "Endoproteolysis of Presenilin 1 and Accumulation of Processed Derivatives In Vivo," <i>Neuron</i> 17:181-190 (July 1996)
KC	AT	17	Thompson, C.B., "Apoptosis in the Pathogenesis and Treatment of Disease," <i>Science</i> 267:1456-1462 (1995)

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0609.4270001	APPLICATION NO. 09/065,902
	APPLICANT TANZI and KIM	
	FILING DATE April 24, 1998	GROUP 1643

JUL 29 1998

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KC	AR	18	Tomita, T., et al., "The presenilin 2 mutation (N141I) linked to familial Alzheimer disease (Volga German families) increases the secretion of amyloid $\beta$ protein ending at the 42nd (or 43rd) residue," <i>Proc. Natl. Acad. Sci. USA</i> 94:2025-2030 (March 1997)
KC	AS	18	Walter, J., et al., "The Alzheimer's Disease-Associated Presenilins Are Differentially Phosphorylated Proteins Located Predominantly within the Endoplasmic Reticulum," <i>Molecular Medicine</i> 2:673-691 (November 1996)
KC	AT	18	Wang, X., et al., "SREBP-1, a Membrane-Bound Transcription Factor Released by Sterol-Regulated Proteolysis," <i>Cell</i> 77:53-62 (1994)

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	APPLICANT TANZI and KIM <b>GROUP 1800</b>	
	FILING DATE April 24, 1998	GROUP <b>1643/1117</b>

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<i>KC</i>	AR	<u>19</u>	Wang, X., et al., "Cleavage of sterol regulatory element binding proteins (SREBPs) by CPP32 during apoptosis," <i>EMBO J.</i> 15:1012-1020 (March 1996)
<i>KC</i>	AS	<u>19</u>	Ward, C.L., et al., "Degradation of CFTR by the Ubiquitin-Proteasome Pathway," <i>Cell</i> 83:121-127 (1995)
<i>KC</i>	AT	<u>19</u>	Wasco, W., and Tanzi, R.E., "Molecular genetics of amyloid and apolipoprotein E in Alzheimer's disease," in <i>Neurobiology of Alzheimer's Disease</i> , Dawbarn, D., and Allen, S.J., eds., Bios Scientific Publishers Limited, Oxford, UK, pp. 51-76 (1995)

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				APPLICANT TANZI and KIM		JUL 29 1998 GROUP 1801	
				FILING DATE April 24, 1998		GROUP 1643	

  

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KC	AR	20	Wiertz, E.J.H.J., <i>et al.</i> , "Sec61-mediated transfer of a membrane protein from the endoplasmic reticulum to the proteasome for destruction," <i>Nature</i> 384:432-438 (December 1996)
KC	AS	20	Wolozin, B., <i>et al.</i> , "Participation of Presenilin 2 in Apoptosis: Enhanced Basal Activity Conferred by an Alzheimer Mutation," <i>Science</i> 274:1710-1713 (December 1996)
KC	AT	20	Xia, W., <i>et al.</i> , "Enhanced Production and Oligomerization of the 42-residue Amyloid $\beta$ -Protein by Chinese Hamster Ovary Cells Stably Expressing Mutant Presenilins," <i>J. Biol. Chem.</i> 272:7977-7982 (March 1997)

  

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	APPLICANT TANZI and KIM	
	FILING DATE April 24, 1998	GROUP 1643 1644

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KC	AR	21	Yankner, B.A., et al., "Neurotrophic and Neurotoxic Effects of Amyloid $\beta$ Protein: Reversal by Tachykinin Neuropeptides," <i>Science</i> 250:279-282 (1990)
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